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THYMIC DEPENDENCE OF TOLERANCE IN VASCULARIZED COMPOSITE TISSUE ALLOGRAFTS UNDER CYCLOSPORINE A AND AB-T CELL RECEPTOR MONOCLONAL ANTIBODY PROTOCOL

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Background: In our previous studies, we have demonstrated that vascularized composite tissue allograft transplants treated with ab-TCR) monoclonal antibody (mAb) and Cyclosporine A (CsA) for 7 days developed robust tolerance across MHC barrier. In this paper we have investigated the role of host thymus in the induction of tolerance in rat hind-limb allograft model.

Material and Methods. Five weeks old, euthymic (group A) and thymectomized (group B) Lewis recipients (LEW,RT1l) received vascularized hind-limb allografts from Lewis-Brown-Norway (LBNfF1, RT1l+n) donors. Group IA (n=6) and IB (n=6) and Group IIA (n=6) and IIB (n=6) served as the isograft and the allograft control groups, respectively. Groups IIIA (n=5) IIIB (n=5) and IVA (n=5) and IVB (n=5) received monotherapies of either ab-TCR mAb or CsA for 7 days, respectively. In Groups VA(n=6) and VB (n=6) a treatment protocol of combined ab-TCR/CsA was applied for 7 days . Mixed lymphocyte reaction (MLR) and skin grafting were performed for the evaluation of the donor specific tolerance in vitro and in vivo, respectively. Flow cytometry analysis was applied for the determination of the efficacy of immunosuppressive treatment and the presence of mixed donor specific, hematopoietic chimerism.

Results. Combined treatment with ab-TCR/CsA protocol resulted in indefinite survival of the euthymic rats from group VB (>100 days) and extended the survival of the animals from group VA up to 51 days, post-transplant. MLR showed donor specific tolerance in the group VA at day 100. Flow cytometry revealed stable, multilinege chimerism in the peripheral blood of euthymic rats (CD4+/RT1n–17.3% and CD8+/RT11n–13.9%) and transient chimerism in thymectiomized limb allograft recipients.

Conclusions: Thymus is necessary for the induction of donor specific tolerance under ab-TCR/CsA protocol in vascularized composite tissue allograft model. Tolerogenic activity of the thymus resulted in the creation of stable mixed hematopoietic macrochimeric state within recipient.

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LACK OF CORRELATION BETWEEN TELOMERE LENGTH AND TELOMERASE ACTIVITY AND EXPRESSION IN LEUKEMIC CELLS

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Telomerase is a ribonucleoprotein complex that allows cells to grow indefinitely and it is believed that reactivation of telomerase plays an important role in immortalization and carcinogenesis. The aim of this work was to analyze the telomerase expression and activity along with telomere length in leukemic cells at the moment of diagnosis and during therapy. Cells were isolated from peri-pheral blood and bone marrow of children with ALL and ANNL. Controls included normal peripheral blood lymphocytes and myeloblast cell line K562. Telomerase expression has been studied by RT-PCR using specific primers for telomerase reverse trancriptase gene (hTERT), telomerase template RNA (hTR) and telomerase associated protein gene (TP1). Telomerase repeat amplification protocol-TRAP and PCR-ELISA (Roche) were used for analysis of telomerase activity. For studying telomere length Telo TAGGG Telomere Length assay (Roche) was used. High telomerase expression